

Chapter 18.4. Refinement at atomic resolution

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18.4.1. The atomic model and a definition of atomic resolution

18.4.1.1. The atomic model

X-rays are diffracted by the electrons that are distributed around the atomic nuclei, and the result of an X-ray crystallographic study is the derived three-dimensional electron-density distribution in the unit cell of the crystal. The elegant simplicity and power of X-ray crystallography arise from the fact that molecular structures are composed of discrete atoms that are treated as spherically symmetric in the usual approximation. This property places such strong restraints on the Fourier transform of the crystal structures of small molecules that the phase problem can be solved by knowledge of the amplitudes alone.

Each atom or ion can be described by up to 11 parameters (Table 18.4.1.1).

The first parameter is the scattering-factor amplitude for the chemical nature of the atom in question, and has been computed and tabulated for all atom types [*International Tables for Crystallography*, Volume C (2004)]. Once the chemical identity of the atom is established, this parameter is fixed.

The next three parameters relate to the positional coordinates of the atom with respect to the origin of the unit cell.

If the resolution is high enough, then the number of observed reflections is sufficient to allow six anisotropic atomic displacement parameters to be used to describe the distribution of the atom positions in different unit cells (Fig. 18.4.1.1). Atomic displacement parameters (ADPs) reflect both the thermal vibration of atoms about the mean position as a function of time (dynamic disorder) and the variation of positions between different unit cells of the crystal arising from its imperfection (static disorder). Contributors to the apparent ADP (U_{atom}) can be thought of as follows (Murshudov *et al.*, 1999):

$$U_{\text{atom}} = U_{\text{crystal}} + U_{\text{TLS}} + U_{\text{torsion}} + U_{\text{bond}}, \quad (18.4.1.1)$$

where U_{crystal} represents the fact that a crystal itself is in general an anisotropic field that will result in the intensity falling off in an anisotropic manner, U_{TLS} represents a translation/libration/screw (TLS), *i.e.* the overall motion of molecules or domains (Schomaker & Trueblood, 1968; Winn *et al.*, 2001), U_{torsion} is the oscillation along torsion angles and U_{bond} is the oscillation along and across bonds. In principle, all these contributors are highly correlated and it is difficult to separate them from one another. Nevertheless, an understanding of how U_{atom} is a sum of these different components makes it possible to apply atomic anisotropy parameters at different resolutions in a different manner. For example, $U_{\text{crystal}} + U_{\text{TLS}}$ can be applied at any resolution, as

their refinement increases the number of parameters by at most five for U_{crystal} and 20 per independent moiety for U_{TLS} . In contrast, refinement of the third contributor does pose a problem, as there is strong correlation between different torsion angles. As an alternative, ADPs along the internal degrees of freedom could in principle be refined. The fourth and final contributor, U_{bond} , can only be refined at very high resolution. In real applications, U_{crystal} and U_{TLS} are separated for convenient description of the system, but in practice their effects are indistinguishable.

In the special case when the tensor U_{atom} is isotropic, *i.e.*, all non-diagonal elements are equal to zero and all diagonal terms are equal to each other, then the atom itself appears to be isotropic and its ADP can be described using only one parameter, U_{iso} .

Thus, for a full description of a crystal structure in which all atoms only occupy a single site, nine parameters per atom must be determined: three positional parameters and six anisotropic ADPs. This assumes that the spherical-atom approximation applies and ignores the so-called deformation density resulting from the non-spherical nature of the outer atomic and molecular orbitals involved in the chemical interactions between the atoms (Coppens, 1997).

For disordered regions or features, where atoms can be distributed over two or more identifiable sites, the occupancy introduces a tenth variable for each atom. In many cases, the fractional occupancies are not all independent, but are rather constant for sets of covalently or hydrogen-bonded atoms or for those in non-overlapping solvent networks. This would apply, for example, to partially occupied ligands or side chains with two conformations.

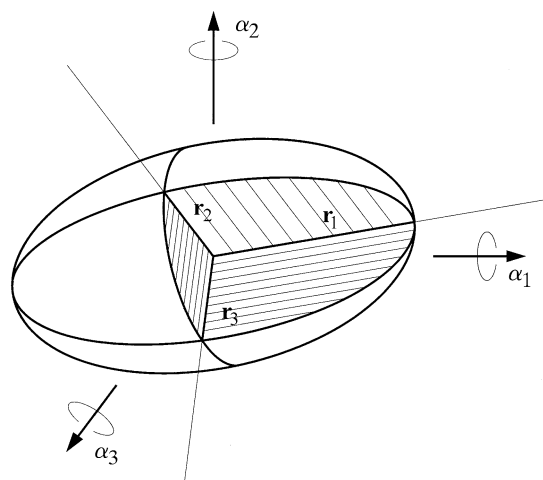


Figure 18.4.1.1

The thermal-ellipsoid model used to represent anisotropic atomic displacement, with major axes indicated. The ellipsoid is drawn with a specified probability of finding an atom inside its contour. Six parameters are necessary to describe the ellipsoid: three represent the dimensions of the major axes and three the orientation of these axes. These six parameters are expressed in terms of a symmetric U tensor and contribute to atomic scattering through the term $\exp[-2\pi^2(U_{11}h^2a^{*2} + U_{22}k^2b^{*2} + U_{33}l^2c^{*2} + 2U_{12}hka^*b^*\cos\gamma^* + 2U_{13}hla^*c^*\cos\beta^* + 2U_{23}klb^*c^*\cos\alpha^*)]$.

Table 18.4.1.1

The parameters of an atomic model

Parameter type	Number	Variable or fixed
Atom type	1	Fixed after identification
Positional (x, y, z)	3	Variable, subject to restraints
ADPs:		
isotropic	1	Variable beyond about 2.5 Å
anisotropic	6	Variable beyond about 1.5 Å
Occupancy	1	Variable for visible disorder